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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/630,215	08/01/2000	John F. O'Connor	54205-A-PCT-US/JPW/SHS/MV	7218

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EXAMINER	
GABEL, GAILENE	
ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 11/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/630,215	O'CONNOR ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-61 and 63-66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *58-61* is/are allowed.

6)☒ Claim(s) *63-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 22, 2005 has been entered.

Amendment Entry

2. Applicant's response filed September 22, 2005 is acknowledged and has been entered. Claims 58-61 and 63-66 are pending and remain under examination.

Withdrawn Rejections

3. In light of Applicant's argument, the rejection of claims 58-61 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of US Patent 6,500,627, is hereby, withdrawn.

New Grounds of Rejection

Conflicting Claims

4. Claims 63-66 of this application conflict with claims 57-61 of Application No. 10/335,115. 37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

Statutory Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

5. Claims 63-66 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 57-61 of ASN 10/335,115. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

6. Claims 63-66 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 57-61 of copending Application No. 10/335,115. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claims 57-61 of copending ASN 10/335,115 recite a diagnostic kit for determining amount of early pregnancy associated molecular isoform of hCG (EPMI-hCG) to predict pregnancy outcome in a subject comprising a first antibody (B152) immobilized to a solid support which binds EPMI-hCG, a second labeled antibody (B207) which binds EPMI-hCG simultaneously, a third antibody (B109) immobilized to a solid support which binds intact non-nicked hCG, a fourth labeled antibody (B108) which binds intact non-nicked hCG simultaneously; and also reagents permitting binding between all the antibodies and the epitopes upon which they bind. These claims are substantially the same claims as those recited in claims 63-66 of the instant invention.

Obviousness Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 63-66 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 53-56 of copending Application No. 10/335,115 in view of in view of Birken et al. (Endocrinology, 1993).

Claims 53-56 of copending ASN 10/335,115 recite a diagnostic kit for determining amount of early pregnancy associated molecular isoform of hCG (EPMI-hCG) to predict pregnancy outcome in a subject comprising a first antibody (B152) immobilized to a solid support which binds EPMI-hCG, a second labeled antibody (B207) which binds EPMI-hCG simultaneously, and reagents permitting binding between the antibodies and EPMI-hCG epitopes upon which they bind.

ASN 10/335,115 is silent in reciting complementary antibodies such as a third antibody (B109) immobilized to a solid support which binds intact non-nicked hCG and a fourth labeled antibody (B108) which binds intact non-nicked hCG simultaneously, to separate the EPMI-hCG analyte from the intact non-nicked hCG analyte as part of the diagnostic kit for determining amount of EPMI-hCG.

Birken et al. teach employing four monoclonal antibodies: B109 and B107 which are both directed to intact non-nicked heterodimer hCG, B108 directed to intact non-nicked hCG heterodimer, free hCG β-subunit and nicked hCG, and B210, specific for the hCG- β core fragment, in a two-site immunoradiometric assay used to evaluate early pregnancy loss and to separate nicked hCG, intact non-nicked hCG, as well as hCG β-

core fragment from reference preparations. In practice, B109 and B210 are immobilized in solid phase as capture antibodies and B108 is labeled with ^{125}I for use as detection antibody in order to separate, detect, and obtain the ratios of analytes including intact non-nicked hCG, nicked hCG, and also hCG β-core fragment (see page 1390 and 1391, column 1).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the monoclonal antibodies taught by Birken with those taught in ASN 10/335,115, because the references are analogous in using the antibodies to bind analytes for detecting early pregnancy outcome or loss based on the amount of a specific analyte present in the patient sample, and in combining the antibodies taught by Birken into the kit of ASN 10/335,115, two analytes that detect for early pregnancy outcome or loss are obtained and ratioed; hence, making for a more accurate assay for detecting early pregnancy outcome or loss. Accordingly, use of four antibodies to detect two distinct analytes simultaneously that provide a determination of early pregnancy outcome or loss is an obvious variation of design choice of assay in the immunological art, for its recognized advantage of specificity and accuracy.

This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 63, 65, and 66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cole et al. (US Patent 6,429,018) in view of Birken et al. (Endocrinology, 1993) and in further view of Foster et al. (US Patent 4,444,879).

Cole et al. disclose a method for determining the amount of an early pregnancy-associated molecular isoform of hCG or EPMI-hCG (prenatal screening for nicked hyperglycosylated gonadotropin in Down's Syndrome cases) in a urine sample using B152 antibody immobilized into solid phase as capture antibody which binds EPMI-hCG or hyperglycosylated gonadotropin, and a second labeled antibody to hCG, β-core fragment of hCG, α-subunit, and/or a β-subunit, which also binds to EPMI-hCG simultaneously with the first antibody. Down's Syndrome cases generally can lead to early pregnancy loss (see column 5, lines 14-18, 42-67, column 6, lines 38-54, and Example 3).

Cole et al. differ from the instant invention in failing to specifically teach B109 as a third antibody immobilized into solid phase as capture antibody and B108 as fourth antibody used as detection label antibody for use in binding intact non-nicked hCG in pregnant subjects.

Birken et al. has been discussed supra.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the monoclonal antibodies taught by Birken with those taught by Cole, because the references are analogous in using their antibodies to bind analytes for detecting early pregnancy outcome or loss based on the amount of a

specific analyte present in the patient sample, and in combining the antibodies taught by Birken into the teaching of Cole, two analytes that detect for early pregnancy outcome or loss are obtained and ratioed; hence, making for a more accurate assay in detecting for early pregnancy outcome or loss. Accordingly, use of four antibodies to detect two distinct analytes simultaneously that provide a determination of early pregnancy outcome or loss is an obvious variation of design choice of assay in the immunological art, for its recognized advantage of specificity and accuracy.

Both of Cole et al. and Birken et al. differ from the instant invention in failing to incorporate the antibodies and reagent into a kit format.

Foster et al. teaches incorporating labels, antibodies, and reagents into a kit format.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the reagents, labels, and antibodies taught by Cole as modified by Birken, into a kit arrangement as taught by Foster, because test kits are conventional and well known in the art for their recognized advantage of convenience and economy.

Response to Arguments

9. Applicant's arguments filed September 22, 2005 have been fully considered but they are not persuasive.

A) Applicant argues that there is no suggestion or motivation to combine the antibodies taught by Birken with those of Cole in a method, and further incorporate the assay reagents and antibodies into a kit format, as taught by Foster.

Applicant's argument is not persuasive because Cole and Birken are combined for their analogous teaching of detecting for early pregnancy loss, using specific antibodies for EPMI-hCG, intact non-nicked, and nicked hCG isoforms, wherein their combination is motivated by increase in specificity and accuracy in using two-site / two analyte simultaneous immunological assay for determining early pregnancy outcome or loss. Additionally, incorporation of all the combined reagents and antibodies in the teachings of Cole and Birken into a kit format as suggested by Cole, is motivated by the recognized advantage of convenience and economy in kit format arrangements.

Prior Art

10. Claims 58-61 and 64 are clear of the prior art of record.

11. Claims 58-61 are allowable.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (571) 272-0820. The examiner can normally be reached on Monday, Tuesday, and Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gailene R. Gabel
Patent Examiner
Art Unit 1641
October 29, 2005